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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/071,822	02/08/2002	Gregory E. Hardee	ISIS-4947	4141

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EXAMINER	
GIBBS, TERRA C	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 07/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/071,822	HARDEE ET AL.	
	Examiner	Art Unit	
	Terra C. Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26 and 27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a response to Applicants Remarks/Arguments filed April 29, 2004. Claims 1-25 and 28 have been canceled. Claims 26 and 27 are pending in the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102

In the previous Office Action mailed January 30, 2004, claims 26 and 27 were rejected under 35 U.S.C. 102(a) as being anticipated by Dean et al. [WO 98/49348]. **This rejection is maintained** for the reasons of record set forth in the previous Office Action.

Response to Arguments

In response to the 35 U.S.C. 102(a) rejection against claims 26 and 27 as being anticipated by Dean et al. [WO 98/49348], Applicants argue that the disclosure of the Dean application is too broad to be anticipatory. Applicants argue that the Dean application discloses certain modified oligonucleotides which are formulated according to methods known in the art and such formulations may include many possible ingredients as detailed throughout the Dean application. Applicants contend that because the compositions recited in the instant claims are not explicitly identified in the Dean application, Applicants surmise that the instant rejection has been entered because the Office is of the view that one skilled in the art could have produced a claimed invention by picking and choosing from among the many possibilities discussed.

Applicants argue that the need for such picking and choosing is plainly inconsistent with a finding of anticipation. Applicants rely on *In re Schaumann*, 572 F.2d 312, 314 (C.C.P.A. 1978). Applicants argue that given the many possible compositions detailed in the Dean application's disclosure, the rejection for alleged anticipation is improper and should be withdrawn.

Applicant's arguments have been fully considered but are not found persuasive because Applicants argue that the Dean application discloses certain modified oligonucleotides which are formulated according to methods known in the art and such formulations may include many possible ingredients as detailed throughout the Dean application. Applicants contend that the compositions recited in the instant claims are not explicitly identified in the Dean application. The Examiner would like to point out that the instant claims are not drawn to compositions, but is instead drawn to a method of delivering a biologically active substance across a mucosal membrane. Dean et al. [WO 98/49348] "the Dean application" explicitly identifies and discloses the methods recited in the instant claims. For example, claim 26 is drawn to a method of delivering a biologically active substance across a mucosal membrane, comprising introducing a nonparenteral multi-particulate formation comprising: a plurality of carrier particles; an oligonucleotide; and a penetration enhancer selected from the groups consisting of a fatty acid, bile salt, chelating agent and non-chelating non-surfactant, wherein said fatty acid is selected from the group consisting of oleic acid, lauric acid, capric acid, myristic acid, palmitic acid, stearic acid, linoleic acid, linolenic acid, dicaprate, tricaprate, moolein, diluarin, caprylic acid, arachidonic acid, glyceryl 1-monocaprate, 1-didecylazacycloheptan-2-one, acylcarnitines, acylcholines, monoglycerides, diglycerides, and salts thereof. Claim 27 is dependent on claim 26 and includes all the limitations of claim 26, with the further limitations, wherein said

biologically active substance is an oligonucleotide and said formulation is administered orally. The Dean application, at Table 1, explicitly identifies the *in vivo* bioavailability of ICAM-1 oligonucleotides in dogs following intrajejunally administration with or without penetration enhancers. The Dean application, at Table 1, further discloses that bile salts (CDCA), were used alone or in combination with fatty acids (2% CDCA, 4% Na caprate, and 4% Na laurate). Dean et al. further disclose that ported, along with naive dogs, were used for the assessment of formulations given by oral administration in which dogs were dosed with oligonucletoide and blood samples were collected and evaluated for the presence and concentration of oligonucleotides, wherein the absolute bioavailability was calculated (see Example 12, for example). Therefore, it is the Examiners position that the Dean application explicitly identifies and discloses the methods recited in the instant claims. Therefore, Dean et al. anticipates claims 26 and 27.

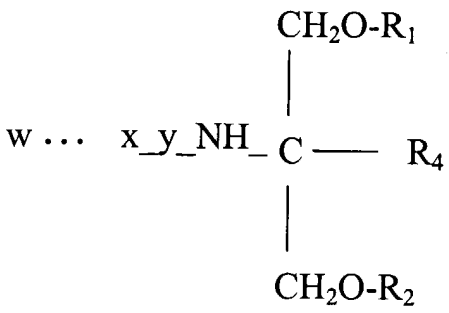
In the previous Office Action mailed January 30, 2004, claims 26 and 27 were rejected under 35 U.S.C. 102(b) as being anticipated by Lockett et al. [WO 97/25339]. **This rejection is maintained** for the reasons of record set forth in the previous Office Action.

Response to Arguments

In response to the 35 U.S.C. 102(b) as being anticipated by Lockett et al. [WO 97/25339], As argued above, Applicants surmise that the instant rejection has been entered because the Office is of the view that one skilled in the art could have produced a claimed invention by picking and choosing from among the many composition possibilities discussed. Applicants

argue that the need for such picking and choosing is plainly inconsistent with a finding of anticipation. Applicants rely on *In re Schaumann*, 572 F.2d 312, 314 (C.C.P.A. 1978). Applicants also argue that the Lockett application teaches introducing its compositions into a cell by exposing the cell to the compositions, and does not discuss administration across a mucosal membrane. Applicants contend that since the Lockett application does not teach every element of the instant claims, the rejection should be withdrawn.

Applicant's arguments have been fully considered but are not found persuasive because as argued above, the instant claims are not drawn to compositions, but is instead drawn to a method of delivering a biologically active substance across a mucosal membrane. Lockett et al. [WO 97/25339] "the Lockett application" explicitly identifies and discloses the methods recited in the instant claims. For example, the Lockett application explicitly claims a method for introducing a nucleic acid into a cell comprising exposing the cell to a compound having the formula:



in which :

w is a nucleic acid, x is a non-amino acid or non-peptide nucleic acid binding group, y is a spacer having a chain length equivalent to 1-30 carbon-carbon single covalent bonds or is

absent, R_4 is H or halogen or CH_2O-R_3; and R_1, R_2, and R_3 are the same or different and are either hydrogen, methyl, ethyl, alkyl, elkenyl, hydroxylated alkyl, hydroxylated alkenyl groups or ether containing alkyl, alkenyl, hydroxylated alkyl or hydroxylated alkenyl groups, optionally being an acyl group derived from a fatty acid having a carbon chain length equivalent to 3-24 carbon atoms saturated or unsaturated, with the proviso that at least one of R_1, R_2 or R_3 include a group having a carbon chain of 3-24 carbon atoms saturated or unsaturated; in which the R_1, R_2, and/or R_3 are cholesterol or acyl derivative of fatty acids selected from the group consisting of palmitate, myristate, laurate, caprate, and oleate; in which the method is conducted *in vivo*; in which the compound is administered orally or by suppository (see claims 1, 5, 10, and 11). Therefore, it is the Examiners position that the Lockett application explicitly identifies and discloses the methods recited in the instant claims.

Applicants also argue that the Lockett application teaches introducing its compositions into a cell by exposing the cell to the compositions, and does not discuss administration across a mucosal membrane. This is not found persuasive because the compositions disclosed by the Lockett application are administered orally or by suppository (see claim 11, for example). One skilled in the art would readily accept that oral or suppository administration would consist of administration across a mucosal membrane as recited in the instant claims. Therefore, the Lockett application anticipates claims 26 and 27.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is (571) 272-0758. The examiner can normally be reached on M-F 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (571) 272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

tcg
July 20, 2004

KAREN A. LACOURCIERE, PH.D
PRIMARY EXAMINER